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(81) Designated States: AL, AM, AT, AT (Utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), EE, EE (Utility model), ES, FI, FI (Utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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With international search report.

(54) Title: GALACTOSYLCERAMIDE, GLUCOSYLCERAMIDE, LACTOSYLCERAMIDE, AND SPECIFIC CATCHERS THEREFOR FOR USE IN THE PROPHYLAXIS OR THERAPY OF PREDIABETES, DIABETES AND/OR ASSOCIATED COMPLICATIONS

(57) Abstract

The use of glycolipids, in particular galactosylceramide, glucosylceramide and lactosylceramide, and specific catchers therefor (antibodies or lectins), in particular monoclonal antibodies, for use in the prophylaxis or therapy of prediabetes, diabetes and/or associated complications in an individual and for use in the production of pharmaceutical preparations for treatment of said conditions is disclosed.

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GALACTOSYLCERAMIDE, GLUCOSYLCERAMIDE, LACTOSYLCERAMIDE, AND SPECIFIC CATCHERS THEREFOR FOR USE IN THE PROPHYLAXIS OR THERAPY OF PREDIABETES, DIABETES AND/OR ASSOCIATED COMPLICATIONS

Technical field of the invention

The present invention relates to the use of glycolipids and specific catchers therefore in treatment of diabetes.

Background of the invention

Galactosylceramide is a glycolipid consisting of ceramide to which galactose is attached. It is made by the enzyme ceramide galactosyltransferase which binds its two parts together. Galactosylceramide is a precursor of sulfatide and is present in the neural system and in islets of Langerhans in small amounts. A sulfatransferase enzyme is able to attach sulfate to the galactose group and thereby to convert galactosylceramide to sulfatide . It is a possibility that galactosylceramide given in vivo is converted to sulfatide. However, galactosylceramide may also act by itself and, indeed effects of galactosylceramide have been described in vitro (Buschard, K., Diamant, M., Bovin, L. F., Fredman, P., Bendtzen, K., Sulphatide and its precursor, galactosylceramide, influence the production of cytokines in human mononuclear cells. APMIS 104: 938-944, 1996). It has been shown that galactosylceramide can modulate and mainly enhance the production of different cytokines from both monocytes and T-cells after stimulation with LPS and PHA, respectively. Most importantly TNF and IL-6 production is increased compared to incubation with LPS and PHA without galactosylceramide.

Glucosylceramide and lactosylceramide are related glycolipids which likely have the same effects as galactosylceramide.

Summary of the invention

The present invention relates to the use of a glycolipid or a specific catcher thereof for the production of a pharmaceutical preparation for treatment of prediabetes, diabetes and/or associated complications in an individual.

Furthermore, the invention relates to glycolipids, in particular galactosylceramide, glucosylceramide and lactosylceramide, and specific catchers therefore (antibodies or lectins) for use in the prophylaxis or therapy of prediabetes, diabetes and/or associated complications in an individual.

The invention also relates to a specific catcher for the glycolipids according to the invention, said catcher being a monoclonal antibody against galactosylceramide, glucosylceramide or lactosylceramide.

The invention also relates to a method for preventing the development of prediabetes, diabetes and/or associated complications in an individual, wherein a glycolipid, in particular galactosylceramide, glucosylceramide or lactosylceramide, is administered to said individual, preferably at its perinatal stage.

The characterising features or the invention will be evident from the following description and the appended claims.

Detailed description of the invention

As stated above, the invention relates glycolipids, in particular galactosylceramide, glucosylceramide and lactosylceramide, and specific catchers therefore (antibodies or lectins) for use in the prophylaxis or therapy of prediabetes, diabetes and/or associated complications in an individual, as well as to the use of a glycolipid or a specific catcher thereof for the production of a pharmaceutical preparation for treatment of

prediabetes, diabetes and/or associated complications in an individual.

The expression "treatment" used herein relates to both the prophylaxis of said conditions in an individual being in risk of developing any of the conditions and to the therapeutic treatment of an individual who have already developed any of the conditions.

The prophylactic treatment is performed by inducing tolerance to the antigenic glycolipids. When the glycolipids, the specific catchers therefore and/or the pharmaceutical preparation according to the invention is used for this purpose they are preferably administered perinatally to said individual.

The glycolipid used according to the invention is preferably galactosylceramide, glucosylceramide or lactosylceramide. The specific catcher used according to the invention is preferably an antibody or a lectin, and more preferably a monoclonal antibody against galactosylceramide, glucosylceramide or lactosylceramide.

The glycolipid, the specific catcher or the pharmaceutical preparation according to the invention may be administered in any suitable way known to the man skilled in the art. Preferably, they are administered nasally, orally, subcutaneously, intramuscularly, or intravenously.

The glycolipids or the pharmaceutical preparation may lead to increased levels of suppressor or regulator cells or antibodies against lymphocytes recognising the antigenic glycolipids in said individual. Alternatively, they may lead to the removal of antibodies and/or lymphocytes recognising the antigenic glycolipids from the blood stream of the individual.

It may be suitable to administer the glycolipids according to the invention together with bacterial adjuvants. The pharmaceutical composition according to the invention may therefore also comprises a least one bacte-

rial adjuvant, such as cholera, staphyloccoc or galactosylceramide (alpha-form) of bacterial origin.

The pharmaceutical preparation according to the invention may also comprise substances used to facilitate the production of the pharmaceutical preparation or the administration of the preparations. Such substances are well known to people skilled in the art and may for example be pharmaceutically acceptable adjuvants, carriers and preservatives.

When antibodies are used according to the invention they will lead to an increase of anti-antibodies in said individual.

The invention also relates to a method for preventing the development of prediabetes, diabetes and/or associated complications in an individual, wherein a glycolipid, in particular galactosylceramide, glucosylceramide or lactosylceramide, is administered to said individual, preferably at its perinatal stage.

The method may be performed by removing lymphocytes from the individual, contact the lymphocytes with a glycolipid, in particular galactosylceramide, glucosylceramide or lactosylceramide, in vitro to make them recognise this antigen, irradiating them to inhibit their cytotoxicity, and (a) returning them to the individual to raise suppressor or regulator cells or antibodies against lymphocytes reactive with this antigen, or (b) administering them parenterally to another mammal in order to raise antibodies against lymphocytes reactive with this antigen in said mammal and then isolating serum containing the antibodies from said mammal and administering it to the individual.

The method may also be performed by contacting the blood stream of the individual with an immobilised glycolipid, in particular galactosylceramide, glucosylceramide or lactosylceramide, to remove antibodies and/or lymphocytes recognising the antigenic glycolipids from the individual.

Finally, it is also possible to perform the method by parenterally administer an antibody against glycolipids, in particular galactosylceramide, glucosylceramide or lactosylceramide, (a) to said individual in a sufficient amount to raise anti-antibodies in said individual, or (b) to another mammal in order to raise anti-antibodies in said mammal and then isolating serum containing the anti-antibodies from said mammal and administering it to the individual.

The invention will now be further explained in the following example. This example is only intended to illustrate the invention and should in no way be considered to limit the scope of the invention.

Example - Treatment of NOD mice with the intrathymic injections of galactosylceramide in order to modulate the later diabetes incidence

Materials and methods

The NOD mouse model is an animal model of type 1 diabetes. The mice develop spontaneously diabetes within 200 days of life with an incidence of 50% or more. In the present study the animals were examined daily and once a week checked for glucosuria. They were diagnosed as diabetic if their blood glucose values was higher than 200 mg glucose per 100 ml. When diagnosed as diabetics the animals were sacrificed. Otherwise the remaining non-diabetic animals were sacrificed at the end 5 of the study after 200 days of age.

Four groups of animals each containing between 30 and 40 animals were investigated. The animals were injected intrathymically when 3 weeks old. There was injected 50 µl galactosylceramide in 100 µl vehicle (PBS). The control mice were treated with the 100 µl PBS alone. In another experiment liposome preparation of galactosylceramide was made using phosphatidylcholin and galactosylceramide. The control group was treated with phosphatidylcholin and PBS alone.

Results

In the first study with treatment of galactosylceramide in pure form 17 of 37 mice (=45.9%) developed diabetes, whereas 21 of 37 (=56.8%) of the control (PBS-treated) mice developed the disease. In the second study with galactosylceramide in liposome form 14 of 33 (=42.4%) of the galactosylceramide liposome treated mice developed diabetes whereas 18 of 31 (=58.1%) of the control (PBS-treated) mice develop the disease.

Taking the two studies together 31 of 70 (=44.3%) of the galactosylceramide treated mice developed diabetes whereas 39 of 68 (=57.4%) of PBS mice developed the disease. In the first study the diabetes development in the galactosylceramide treated group occurred later than among the control mice.

CLAIMS

1. Use of a glycolipid or a specific catcher thereof for the production of a pharmaceutical preparation for treatment of prediabetes, diabetes and/or associated complications in an individual.

2. Use according to claim 1, wherein said glycolipid is galactosylceramide, glucosylceramide and lactosylceramide.

3. Use according to claim 1 or 2, wherein said specific catcher is an antibody or a lectin.

4. Use according to any one of the claims 1-3, wherein said pharmaceutical preparation is formulated for nasal, oral, subcutaneous, intramuscular, or intravenous administration.

5. Use according to any one of the claims 1-4, wherein said pharmaceutical preparation is intended for the prophylaxis of prediabetes, diabetes and/or associated complications in an individual being in risk of developing said disease, by inducing tolerance to the antigenic glycolipids.

6. Use according to claim 5, wherein said pharmaceutical preparation is intended for perinatal administration thereof to said individual.

7. Use according to any one of the claims 1-6, wherein said pharmaceutical preparation upon administration to an individual will lead to increased levels of suppressor or regulator cells or antibodies against lymphocytes recognising the antigenic glycolipids in said individual.

8. Use according to any one of the claims 1-6, wherein said pharmaceutical preparation upon administration to an individual will lead to the removal of antibodies and/or lymphocytes recognising the antigenic glycolipids from the blood stream of the individual.

9. Use according to any one of the claims 1-8, wherein said pharmaceutical preparation further comprises a least one bacterial adjuvant.

10. Use according to claim 9, wherein said bacterial adjuvant is cholera, staphyloccoc or galactosylceramide (alpha-form) of bacterial origin.

11. Glycolipids, in particular galactosylceramide, glucosylceramide and lactosylceramide, and specific catchers therefore (antibodies or lectins) for use in the prophylaxis or therapy of prediabetes, diabetes and/or associated complications in an individual.

12. Galactosylceramide, glucosylceramide or lactosylceramide for use in the prophylaxis or therapy of prediabetes, diabetes and/or associated complications in an individual given nasally, orally, subcutaneously, intramuscularly, intravenously or otherwise.

13. Glycolipids according to claim 11 or 12, for use in the prophylaxis of prediabetes, diabetes and/or associated complications in an individual being in risk of developing said disease, by inducing tolerance to the antigenic glycolipids, for example by perinatal administration thereof to said individual.

14. Glycolipids according to claim 11 or 12, for use in the prophylaxis or therapy or prediabetes, diabetes and/or associated complications in an individual by raising suppressor or regulator cells or antibodies against lymphocytes recognising the antigenic glycolipids in said individual.

15. Glycolipids according to claim 11 or 12, for use in the prophylaxis or therapy of prediabetes, diabetes and/or associated complications in an individual by removing antibodies and/or lymphocytes recognising the antigenic glycolipids from the blood stream of the individual.

16. Glycolipids according to any one of the claims 11-15 given to an individual together with bacterial ad-

juvants, for example cholera, staphyloccoc or galactosylceramide (alpha-form) of bacterial origin.

17. A specific catcher for glycolipids according to any of claims 11-16, said catcher being a monoclonal antibody against galactosylceramide, glucosylceramide or lactosylceramide.

18. Antibody according to any of claims 11 and 17, for use in the prophylaxis or therapy of prediabetes, diabetes and/or associated complications in an individual by raising anti-antibodies in said individual.

19. A method for preventing the development of prediabetes, diabetes and/or associated complications in an individual, wherein a glycolipid, in particular galactosylceramide, glucosylceramide or lactosylceramide, is administered to said individual, preferably at its perinatal stage.

20. A method for preventing or treating prediabetes, diabetes and/or associated complications in an individual, wherein lymphocytes are removed from the individual, contacted with a glycolipid, in particular galactosylceramide, glucosylceramide or lactosylceramide, in vitro to make them recognise this antigen, irradiating the lymphocytes to inhibit their cytotoxicity, and (a) returning them to the individual to raise suppressor or regulator cells or antibodies against lymphocytes reactive with this antigen, or (b) administering them parenterally to another mammal in order to raise antibodies against lymphocytes reactive with this antigen in said mammal and then isolating serum containing the antibodies from said mammal and administering it to the individual.

21. A method of preventing or treating prediabetes, diabetes and/or associated complications in an individual, wherein the blood stream of the individual is contacted with an immobilised glycolipid, in particular galactosylceramide, glucosylceramide or lactosylceramide, to remove antibodies and/or lymphocytes recognising the antigenic glycolipids from the individual.

22. A method of preventing or treating prediabetes, diabetes and/or associated complications in an individual, wherein an antibody against glycolipids, in particular galactosylceramide, glucosylceramide or lactosylceramide, is parenterally administered (a) to said individual in a sufficient amount to raise anti-antibodies in said individual, or (b) to another mammal in order to raise anti-antibodies in said mammal and then isolating serum containing the anti-antibodies from said mammal and administering it to the individual.

23. A method according to any on of the claims 19-21, wherein the glycolipid is selected from the group consisting of galactosylceramide, glucosylceramide, or lactosylceramide.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 98/02407

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: A61K 31/70, A61K 39/00, C07H 15/04, C07H 15/10
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61K, C07H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS, WPI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 9219633 A1 (BUSCHARD, KARSTEN), 12 November 1992 (12.11.92), See claims	1-23
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X	APMIS, Volume 104, 1996, Karsten Buschard et al, "Sulphatide and its precursor galactosylceramide influence the production of cytokines in human mononuclear cells" page 938 - page 944	11-16
A		1-10,17-23
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A	WO 9742974 A1 (BUSCHARD, KARSTEN), 20 November 1997 (20.11.97)	1-23
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☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
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Date of the actual completion of the international search	Date of mailing of the international search report
7 April 1999	20 -04- 1999
Name and mailing address of the ISA Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. + 46 8 666 02 86	Authorized officer Nebil Gecer Telephone No. + 46 8 782 25 00

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INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 19-23
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 19-23 relate to methods of treatment of the human or animal body by surgery or by therapy/diagnostic methods practised on the human or animal body/Rule 39.1(iv). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compounds/compositions.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

02/03/99

International application No.
PCT/SE 98/02407

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9219633 A1	12/11/92	AT 175203 T	15/01/99
		AU 1788892 A	21/12/92
		DE 69228061 D	00/00/00
		EP 0584175 A,B	02/03/94
		JP 6506943 T	04/08/94
		US 5827828 A	27/10/98
WO 9742974 A1	20/11/97	AU 2918897 A	05/12/97
		SE 9601817 D	00/00/00

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(57) Abstract

The use of glycolipids, in particular galactosylceramide, glucosylceramide and lactosylceramide, and specific catchers therefor (antibodies or lectins), in particular monoclonal antibodies, for use in the prophylaxis or therapy of prediabetes, diabetes and/or associated complications in an individual and for use in the production of pharmaceutical preparations for treatment of said conditions is disclosed.

*(Referred to in PCT Gazette No. 23/2000, Section II)

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EE	Estonia	LR	Liberia	SG	Singapore		

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61K, C07H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS, WPI

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A		1-10,17-23
A	WO 9742974 A1 (BUSCHARD, KARSTEN), 20 November 1997 (20.11.97)	1-23

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
7 April 1999	20 -04- 1999
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Nebil Gecer Telephone No. +46 8 782 25 00

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INTERNATIONAL SEARCH REPORT

International application No.
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0579196 A1 (THE NISSHIN OIL MILLS, LTD.), 19 January 1994 (19.01.94) --	11,13-16
X	EP 0133170 A2 (KARLSSON, KARL-ANDERS), 13 February 1985 (13.02.85) --	11-16
X	US 5242800 A (VICTOR E. JIMENEZ ET AL), 7 Sept 1993 (07.09.93), see column 5, lines 10-11 --	17-18
X	STN International, File Medline, Medline accession no. 97032815, Document no. 97032815, Sosa M A et al: "A human kidney cDNA which induces a cell surface protein epitope recognized by a monoclonal antibody against galactosylceramide"; & Biochemical and Biophysical research communications, (1996 Oct 14) 227 (2) 636-41 --	17-18

INTERNATIONAL SEARCH REPORT

Information on patent family members

02/12/99

Internauonal application No.

PCT/SE 98/02407

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9219633 A1	12/11/92	AT 175203 T	15/01/99
		AU 1788892 A	21/12/92
		DE 69228061 D,T	27/05/99
		EP 0584175 A,B	02/03/94
		SE 0584175 T3	
		ES 2125898 T	16/03/99
		JP 6506943 T	04/08/94
		US 5827828 A	27/10/98
WO 9742974 A1	20/11/97	AU 2918897 A	05/12/97
		EP 0928201 A	14/07/99
		SE 9601817 D	00/00/00
EP 0579196 A1	19/01/94	SE 0579196 T3	
		AT 138383 T	15/06/96
		CA 2100412 A	16/01/94
		DE 69302767 D,T	14/11/96
		DK 579196 T	01/07/96
		ES 2090790 T	16/10/96
		JP 6080687 A	22/03/94
		US 5369096 A	29/11/94
EP 0133170 A2	13/02/85	AU 581850 B	09/03/89
		AU 3049384 A	17/01/85
		DK 347384 A	16/01/85
		FI 842814 A	16/01/85
		JP 60064993 A	13/04/85
		SE 8304006 D	00/00/00
US 5242800 A	07/09/93	NONE	